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Case Report

Carbamazepine induced Stevens-Johnson syndrome: a case report

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Abstract

Stevens-Johnson syndrome (SJS) is a very rare, acute, serious and potentially fatal skin reaction disease. Carbamazepine is one of its most common cause, others are antiretroviral drugs, anti-tuberculosis drugs, sulphonamides, fluoroquinolones, penicillins, non-steroidal anti-inflammatory drugs and multivitamins. Genetic susceptibility has been suggested as a possible explanation. We report a case of SJS secondary to carbamazepine in a patient with previous history of skin rashes due to carbamazepine which was given for treatment of schizoaffective disorder. We would like to highlight that carbamazepine re-administration should be avoided in the patient with a previous history of adverse skin reaction or SJS. In addition, gradual titration and observation for these side effects are recommended while initiating treatment with carbamazepine.

Key words

Adverse effects, carbamazepine, drug eruptions, drug hypersensitivity syndrome, Stevens-Johnson syndrome, toxic epidermal necrolysis

Introduction

Carbamazepine is associated with several dermatological adverse effects including rashes, urticaria, and photosensitivity reactions, whereas, severe and life threatening acute adverse cutaneous drug reactions such as erythema multiforme, toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS) are reported rarely. TEN is clinically characterized by erythematous macules and targeted lesions throughout the body along with more than 30 percent of body surface area having full thickness epidermal necrosis; whereas SJS have less than 10% body surface area affected with full-thickness epidermal necrosis with detachment along with mucous membrane involvement in two or more areas.[1] Most of the reported cases of SJS occur during first two months of antiepileptic drugs use. The estimated risk ranges between one and ten cases per 10,000 new users for carbamazepine, lamotrigine, phenytoin, phenobarbital, whereas lower rates have been reported for valproate.[2] Highest rates of SJS have been reported to occur with carbamazepine around 14/10,000 users.[2,3]

SJS is a clinical syndrome presumed to be a hypersensitivity reaction manifested initially with prodromal symptoms of fever, malaise and a sore throat. The prodromal phase is then followed up to 14 days by an acute polymorphous dermatologic syndrome manifested as erythematous maculo-papular skin lesions, target lesions, bullae, vesicle, involvement of at least two mucus membranes, conjunctivitis and associated systemic toxic state.[4] SJS is severe, acute mucocutaneous reactions that are most often elicited by drugs and occasionally by infections. They are now considered to be differing only in the extent of body surface area involved.[5] The drugs commonly implicated as the cause of SJS are anticonvulsants, sulfonamides, non-steroidal anti-inflammatory drugs and antibiotics.[6,7,8] Carbamazepine is prescribed in schizoaffective disorder and bipolar disorder as a mood stabilizer, and in seizure disorders, trigeminal neuralgia and chronic pain. It is associated with hypersensitivity reactions that range from benign urticaria to life-threatening cutaneous disorders, including SJS and TEN.[4,9,10] In psychiatry, cutaneous adverse drug eruptions are rarely noticed with atypical antipsychotics. To date, very few skin rashes and eruptions with olanzapine have been described in the literature. Dermatological side effects that have been reported with olanzapine are eruptive xanthomas, skin hyperpigmentation and purpura associated with thrombocytopenia.[11] Amongst other atypical antipsychotics, only two cases of erythema multiforme have been reported, one with ziprasidone,[12] and one with risperidone.[13] The SJS carry a mortality that can be as high as 30% and require early diagnosis, with prompt withdrawal of all suspected potential causative drugs.

Case History

A 60-year-old married male patient diagnosed with schizoaffective disorder, presented with increased talk, disturbed sleep and hyperactivity for past 3 months, following treatment with carbamazepine 200mg twice daily along with olanzapine 10mg twice daily. There was no family history of any psychiatric or physical illness, or drug reactions. Further history revealed that he had

discontinued medications including carbamazepine three years back on his own due to mild rash. Then he had many psychotic and manic episodes, and had tried many mood stabilizers: lithium, sodium valproate and lamotrigine but did not get good result. In the past, he had improved with carbamazepine, so carbamazepine was restarted 200mg once daily. On his second day of medication, he had a mild fever and general weakness along with flushing of face and subsequently developed maculopapular rashes, starting from face spreading to neck then trunk and later developed to both legs, on 10th day. On physical examination the patient had pruritic and stinging erythema and red maculopapular rashes on both legs (Figure-1). Pharynx, eyes and genital mucosa were not involved. Nikolsky's sign (mechanical pressure to the skin leading to blistering within minutes or hours) was positive. Laboratory examinations revealed high erythrocyte sedimentation rate 50 mm in the first hour; leukocyte count was 8000 per cubic milliliter; and other investigations were within normal limits.

All his medications were stopped and referred to dermatology department for further management. A diagnosis of drug-induced SJS was made by dermatologist. He was treated with dexamethasone injection 4 mg twice a day, ceftriaxone injection 1 gram twice a day and topical betamethasone. After 17 days his condition improved. Patient had a satisfactory recovery; and at the time of discharge, he had generalized desquamation and incomplete peeling of the skin on the trunk and both legs. He was reviewed in psychiatric department and was started with sodium valproate 1000 mg and olanzapine 10 mg per day. After three weeks, there was complete resolution of manic symptoms. There were no adverse effects.

Discussion

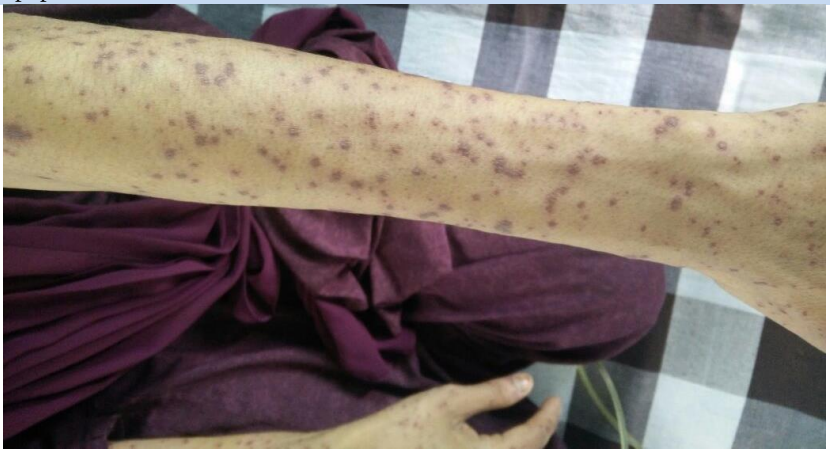
Carbamazepine has been strongly associated with SJS. Although it has multiple etiologies, it is commonly triggered by viral infections (herpes simplex virus is the infectious agent more commonly involved) and neoplasias (carcinomas and lymphomas).[14] However, the most common cause is the use of medications. Among the drugs implicated more often are allopurinol, antibiotics, anticonvulsants and non-steroidal anti-inflammatories. Recently, in a seven-year study, Devi et al. concluded that anticonvulsants were implicated in most cases of SJS especially in the first eight weeks of treatment; and the main drug responsible was carbamazepine.[2]

Typically, the initial presentation is marked by symptoms of fever, myalgia, and general weakness for 1 to 3 days before the development of cutaneous lesions. The skin lesions are symmetrically distributed on the face and upper trunk areas. The rash spreads rapidly and is usually maximal within four days, sometimes within hours. The initial skin lesions are usually poorly defined macules with darker purpuric centers that coalesce. Diagnosis is arrived at through clinical history and examination. However, skin biopsy helps to confirm the diagnosis, usually excluding bullous diseases not related to drug therapy. The patient in this case was exposed to carbamazepine twice; had mild rash in the first exposure few years back; but the degree of his cutaneous reaction was greater with the second exposure, when he developed SJS. Adverse reactions to drugs are reported to increase with age.[15] SJS is reported to affect females more frequently than males, but an Indian study showed a slight male preponderance.[16] Although SJS appears in all age groups but it is more common in older people, probably because of tendency to use more drugs. Most patients are in the second to fourth decades and onwards.[17] Mortality was observed more commonly in elderly patients.[18] It is possible that severity of SJS is greater at extreme of ages perhaps due to poor immune response as compared to adults.[19]

Conclusion

Considering this case report of SJS associated with carbamazepine, it is suggested that carbamazepine re-administration should be avoided in patients with a previous history of rash or SJS. In this regard, obtaining an accurate medical history is important. In addition, it is advisable to observe for any side effects while gradual titrating the dose at the start of treatment with carbamazepine. Awareness about drugs causing serious drug reactions such as SJS and TEN will help doctors prevent such reactions by judicious use of drugs and managing them adequately, reducing associated morbidity and mortality.

Figure1: Red, maculopapular rashes



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